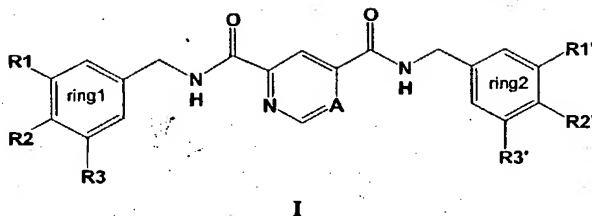


Claims

[c1]

We claim:

A compound of formula I :



wherein

A is a carbon atom or nitrogen atom;

R1 and R3 are independently selected from the group consisting of

hydrogen,

halogen,

-(C1-C4)-alkyl, in which alkyl is unsubstituted or substituted once, twice or three times by halogen, -O-(C1-C4)-alkyl, in which alkyl is unsubstituted or substituted once, twice or three times by halogen,

-C(O)-O-R4,

-CN,

-N(R5)-(R6),

-OH,

-S-(C1-C4)-alkyl,

-S(O)-(C1-C4)-alkyl and

-S(O)₂-R7, and

R2 is selected from the group consisting of

hydrogen,

halogen,

-(C1-C4)-alkyl,

-O-(C1-C4)-alkyl,

-C(O)-O-R4,

-CN,

-N(R5)-(R6),

-OH,

-S-(C1-C4)-alkyl,

-S(O)-(C1-C4)-alkyl and

-S(O)₂-R₇; or R₁ and R₂, taken together with the two carbon atoms of ring1 to which R₁ and R₂ are attached, form a 5- or 6-membered ring which is aromatic or saturated and contains zero, one or two heteroatoms which are independently selected from the group consisting of oxygen, nitrogen and sulfur while R₃ is as defined above; or R₂ and R₃, taken together with the two carbon atoms of ring1 to which R₂ and R₃ are attached, form a 5- or 6-membered ring which is aromatic or saturated and contains zero, one or two heteroatoms which are independently selected from the group consisting of oxygen, nitrogen and sulfur while R₁ is not part of a ring and is as defined above;

R₁' and R₃' are independently selected from the group consisting of hydrogen,

halogen,

-(C1-C4)-alkyl, in which alkyl is unsubstituted or substituted once, twice or three times by halogen,

-O-(C1-C4)-alkyl, in which alkyl is unsubstituted or substituted once, twice or three times by halogen,

-C(O)-O-R₄,

-CN,

-N(R₅)-(R₆),

-OH,

-S-(C1-C4)-alkyl,

-S(O)-(C1-C4)-alkyl and

-S(O)₂-R₇, and

R₂' is selected from the group consisting of hydrogen,

halogen,

-(C1-C4)-alkyl,

-O-(C1-C4)-alkyl,

-C(O)-O-R₄,

-CN,

-N(R₅)-(R₆),

-OH,

-S-(C1-C4)-alkyl,

-S(O)-(C1-C4)-alkyl and

-S(O)₂-R₇; or R₁' and R₂', taken together with the two carbon atoms of ring₂ to which R₁' and R₂' are attached, form a 5- or 6-membered ring which is aromatic or saturated and contains zero, one or two heteroatoms which are independently selected from the group consisting of oxygen, nitrogen and sulfur while R₃' is as defined above; or R₂' and R₃', taken together with the two carbon atoms of ring₂ to which R₂' and R₃' are attached, form a 5- or 6-membered ring which is aromatic or saturated and contains zero, one or two heteroatoms which are independently selected from the group consisting of oxygen, nitrogen and sulfur while R₁' is not a number of a ring and is as defined above;

R₄ is hydrogen or (C1-C4)-alkyl;

R₅ and R₆ are independently selected from the group consisting of hydrogen,

-(C1-C4)-alkyl,

-C(O)-(C1-C4)-alkyl and

-SO₂-(C1-C4)-alkyl; and

R₇ is selected from the group consisting of

-(C1-C4)-alkyl,

OH and

NH₂;

provided that at least one of the radicals R₁, R₂, R₃, R₁', R₂', R₃' is not selected from the group consisting of hydrogen, halogen, nitro, -(C1-C4)-alkyl and -O-(C1-C4)-alkyl.

[c2] A related chemical entity of a compound of claim 1.

[c3] A compound of claim 1, wherein R₁, R₃, R₁', R₃' are not selected from the group consisting of halogen, unsubstituted -(C1-C4)-alkyl and unsubstituted -O-(C1-C4)-alkyl except when there is a 5- or 6-membered ring formed between R₁ and R₂, or between R₂ and R₃, or between R₁' and R₂', or between R₂' and R₃', then R₁, R₃, R₁', R₃' are the same as defined in claim 1.

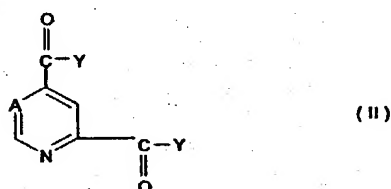
[c4] A compound of claim 1, wherein R1, R3, R1', and R3' are independently selected from the group consisting of hydrogen, chlorine, fluorine, trifluoromethyl, methoxy, methyl, -C(O)-OH, -C(O)-O-CH3, -CN, -NH2, -NH-C(O)-CH3, -NH-SO2-CH3, -N-(CH3)2, -SO2-NH2, -OH, -O-CH2-(CHF2), -S-CH3, -S(O)-CH3, -S(O)2-CH3 and bromine; and R2 and R2' are independently selected from the group consisting of hydrogen, chlorine, fluorine, methoxy, methyl, bromine, -C(O)-OH, -C(O)-O-CH3, -CN, -NH2, -NH-C(O)-CH3, -NH-SO2-CH3, -N-(CH3)2, -SO2-NH2, -OH, -O-CH2-(CHF2), -S-CH3, -S(O)-CH3 and -S(O)2-CH3; or R1 and R2, R2 and R3, R1' and R2', or R2' and R3', together with the two carbon atoms of ring1 or ring2 to which R1 and R2, R2 and R3, R1' and R2', or R2' and R3' are attached, form a dioxolane, dihydrofuran or furan ring, and any R1, R2, R3, R1', R2', or R3' that are not a member of said dioxolane, dihydrofuran or furan ring are the same as defined in the first part of this claim.

[c5] A compound of claim 1, wherein R1, R3, R1', and R3' are independently selected from the group consisting of hydrogen, -(C1-C4)-alkyl, in which alkyl is substituted once, twice or three times by halogen, and -O-(C1-C4)-alkyl, in which alkyl is substituted once, twice or three times by halogen, and R2 and R2' are independently selected from the group consisting of hydrogen, halogen, -O-(C1-C4)-alkyl, and -(C1-C4)-alkyl; or R1 and R2, R2 and R3, R1' and R2', or R2' and R3', together with the two carbon atoms of ring1 or ring2 to which R1 and R2, R2 and R3, R1' and R2', or R2' and R3' are attached, form a 5- or 6-membered ring which is aromatic or saturated and contains zero, one or two heteroatoms which are independently selected from the group consisting of oxygen, nitrogen and sulfur, and any R1, R2, R3, R1', R2', or R3' that are not a member of said a 5- or 6-membered ring are independently selected from the group consisting of hydrogen, halogen, -(C1-C4)-alkyl, in which alkyl is unsubstituted or substituted once, twice or three times by halogen, and -O-(C1-C4)-alkyl, in which alkyl is unsubstituted or substituted once, twice or three times by halogen.

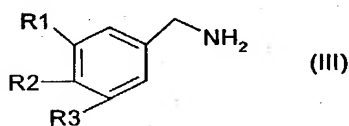
[c6] A compound of claim 1, wherein R1, R3, R1', and R3' are independently selected from the group consisting of hydrogen and trifluoromethyl, and R2 and R2' are independently selected from the group consisting of hydrogen, chlorine,

fluorine, methoxy and methyl; or R1 and R2, R2 and R3, R1' and R2', or R2' and R3', together with the two carbon atoms of ring1 or ring2 to which R1 and R2, R2 and R3, R1' and R2', or R2' and R3' are attached, form a dioxolane, dihydrofuran or furan ring, and any R1, R2, R3, R1', R2', or R3' that are not a member of said dioxolane, dihydrofuran or furan ring are independently selected from the group consisting of hydrogen, chlorine, fluorine, trifluoromethyl, methoxy, and methyl.

- [c7] A process for preparing the compound of formula I as defined in Claim 1, comprising: reacting a compound of formula II

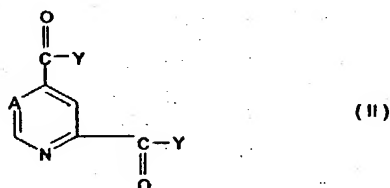


with a compound of formula III

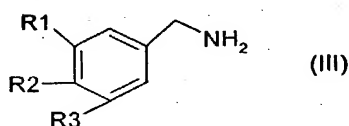


wherein R1, R2 and R3 have the meanings given in claim 1 and Y is halogen, hydroxyl or -(C1-C4)-alkoxy or, together with the carbonyl group to which Y is attached, forms an active ester or a mixed anhydride, to afford a compound of formula I defined in claim 1 wherein R1', R2' and R3' are the same as R1, R2 and R3, respectively.

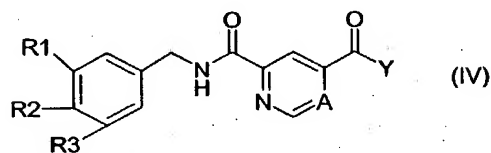
- [c8] A process for preparing the compound of formula I as defined in Claim 1, comprising: reacting a compound of formula II



with a compound of formula III

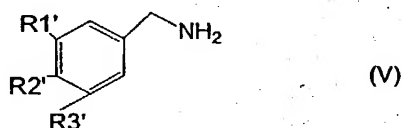


wherein R1, R2 and R3 have the meanings given in claim 1 and Y is halogen, hydroxyl or -(C1-C4)-alkoxy or, together with the carbonyl group to which Y is attached, forms an active ester or a mixed anhydride, to afford an intermediate compound of formula IV



; and

reacting said intermediate compound of formula IV with a compound of formula V

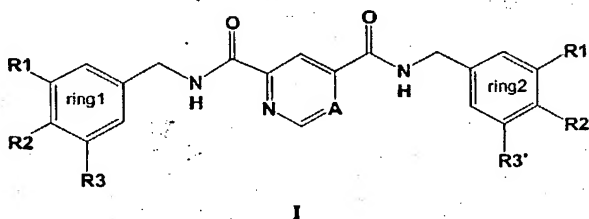


to afford a compound of formula I as defined in claim 1.

[c9] A pharmaceutical composition which comprises an effective amount of at least one compound of claim 1 together with a pharmaceutically suitable and physiologically tolerated carrier substance.

[c10] A pharmaceutical composition which comprises an effective amount of at least one chemical entity of claim 2 together with a pharmaceutically suitable and physiologically tolerated carrier substance.

[c11] A method for prophylaxis and therapy of diseases whose course involves an increased activity of matrix metalloproteinase 13 by using a compound of formula I or a related chemical entity of the compound:



wherein

A is a carbon atom or nitrogen atom;

R1 and R3 are independently selected from the group consisting of
hydrogen,

halogen,

-(C1-C4)-alkyl, in which alkyl is unsubstituted or substituted once, twice or
three times by halogen,

-O-(C1-C4)-alkyl, in which alkyl is unsubstituted or substituted once, twice or
three times by halogen,

-C(O)-O-R4,

-CN,

-N(R5)-(R6),

-OH,

-S-(C1-C4)-alkyl,

-S(O)-(C1-C4)-alkyl and

-S(O)₂-R7, and

R2 is selected from the group consisting of
hydrogen,

halogen,

-(C1-C4)-alkyl,

-O-(C1-C4)-alkyl,

-C(O)-O-R4,

-CN,

-N(R5)-(R6),

-OH,

-S-(C1-C4)-alkyl,

-S(O)-(C1-C4)-alkyl and

-S(O)₂-R7; or R1 and R2, taken together with the two carbon atoms of ring1 to
which R1 and R2 are attached, form a 5- or 6-membered ring which is aromatic
or saturated and contains zero, one or two heteroatoms which are
independently selected from the group consisting of oxygen, nitrogen and
sulfur while R3 is as defined above; or R2 and R3, taken together with the two
carbon atoms of ring1 to which R2 and R3 are attached, form a 5- or 6-
membered ring which is aromatic or saturated and contains zero, one or two
heteroatoms which are independently selected from the group consisting of

oxygen, nitrogen and sulfur while R1 is not part of a ring and is as defined above;

R1' and R3' are independently selected from the group consisting of

hydrogen,

halogen,

-(C1-C4)-alkyl, in which alkyl is unsubstituted or substituted once, twice or three times by halogen,

-O-(C1-C4)-alkyl, in which alkyl is unsubstituted or substituted once, twice or three times by halogen,

-C(O)-O-R4,

-CN,

-N(R5)-(R6),

-OH,

-S-(C1-C4)-alkyl,

-S(O)-(C1-C4)-alkyl and

-S(O)₂-R7, and

R2' is selected from the group consisting of

hydrogen,

halogen,

-(C1-C4)-alkyl,

-O-(C1-C4)-alkyl,

-C(O)-O-R4,

-CN,

-N(R5)-(R6),

-OH,

-S-(C1-C4)-alkyl,

-S(O)-(C1-C4)-alkyl and

-S(O)₂-R7; or R1' and R2', taken together with the two carbon atoms of ring2 to which R1' and R2' are attached, form a 5- or 6-membered ring which is aromatic or saturated and contains zero, one or two heteroatoms which are independently oxygen, nitrogen and sulfur while R3' is as defined above; or R2' and R3', taken together with the two carbon atoms of ring2 to which R2' and R3' are attached, form a 5- or 6-membered ring which is aromatic or saturated and

contains zero, one or two heteroatoms which are independently selected from the group consisting of oxygen, nitrogen and sulfur while R1' is not a number of a ring and is as defined above;

R4 is hydrogen or (C1-C4)-alkyl;

R5 and R6 are independently selected from the group consisting of hydrogen, (C1-C4)-alkyl, -C(O)-(C1-C4)-alkyl and -SO₂-(C1-C4)-alkyl; and

R7 is selected from the group consisting of -(C1-C4)-alkyl, OH and NH₂.

- [c12] A method for prophylaxis and therapy of diseases whose course involves an increased activity of matrix metalloproteinase 13 by using a compound of formula I as defined in claim 1 or a related chemical entity of the compound.
- [c13] A method according to claim 12, wherein said formula I is as defined in claim 3.
- [c14] A method according to claim 12, wherein said formula I is as defined in claim 4.
- [c15] A method according to claim 12, wherein said formula I is as defined in claim 5.
- [c16] A method according to claim 12, wherein said formula I is as defined in claim 6.
- [c17] A method according to claim 11, wherein said diseases are degenerative joint diseases.
- [c18] A method according to claim 17, wherein said degenerative joint diseases include osteoarthroses, osteoarthritis, spondyloses, chondrolysis following joint trauma or a relatively long period of joint immobilization following injuries to the meniscus or patella or tearing of a ligament.
- [c19] A method according to claim 11, wherein said diseases are diseases of connective tissues.
- [c20] A method according to claim 19, wherein said diseases of connective tissues include collagenoses, periodontal diseases and wound healing disturbances.
- [c21] A method according to claim 11, wherein said diseases are chronic diseases of locomotor system.
- [c22] A method according to claim 21, wherein said chronic diseases of locomotor

system include inflammatory, immunologically or metabolism-determined acute and chronic arthritides, arthropathies, myalgias and disturbances of bone metabolism.

[c23] A method according to claim 11 wherein said diseases are cancer diseases including breast cancer.